Amendment #1
to RFP-NIH-NIAID-DAIDS-03-13

"HLA Typing and Epitope Mapping Relative to HIV Vaccine Design"

Amendment to Solicitation No.:	NIH-NIAID-DAIDS-03-13
Amendment No.:	One (1)
Amendment Date:	August 29, 2002
RFP Issue Date:	May 30, 2002
Proposal Due Date: (Changed)	**October 1, 2002 at 4:00 PM Local Time**
Issued By:	Paul D. McFarlane Senior Contracting Officer NIH/NIAID Contract Management Branch 6700-B Rockledge Drive Room 2230, MSC 7612 Bethesda, Maryland 20892-7612
Point of Contact:	Scott Drega, Contract Specialist Sdrega@niaid.nih.gov
Name and Address of Offeror:	To All Offerors
Purpose of Amendment:	See below.

The purpose of this amendment is to provide all Offerors with additional information resulting from issues raised by some potential Offerors. **Also, the date and time for receipt of proposals is extended.**

NIAID received an inquiry regarding the structure and features of the NIAID database maintained to receive the HLA typing data. Offerors are informed that the HLA typing database is actually maintained by the Los Alamos National Laboratories (LANL). The specific issue is restated below and a response is provided thereafter.

Issue:
Our request is for further information regarding the structure and technical features of the NIAID database that is maintained to receive HLA typing, Epitope mapping, immunologic and virologic data, cellular immunity assay data, binding assay data, viral sequencing data, and all other pertinent data that has been collected by the incumbent of this contract, and data that will be gathered and delivered to the NIAID system as part of this future contract activity. It would be very helpful to know the particulars before designing a mechanism for "dumping" data into the NIAID system.

More specifically, if there is need for parallel data structures, in order to allow for seamless merging of data into your current data set, it would be helpful to know the current NIAID HLA database formats. It would also be of particular interest to know if a bar coding system was or is in place for repository activities, and the equipment used for this process, so as to provide parallel data formats.

Response:
Once a contract is awarded, the awarded contractor shall submit, with each annual report to the NIAID, NIH, an electronic listing of optimally defined epitopes identified in the study should be submitted to the database (btk@lanl.gov). This listing should be provided annually regardless of publication status of the epitopes, and can be listed as a personal communication if they aren't yet in the literature. In the past,

publication in the database as a personal communication has in no way precluded publication in the literature, for either sequences or epitopes. If a publication appears between annual reports, the database manager would appreciate notification of the publication. The following specifics regarding the LANL database are also provided.

PART I: WELL-DEFINED EPITOPES:

The epitope listing should contain the following elements, if they are available. Some of these fields would be common to all epitopes in the study and could simply be summarized at the beginning of the file. If no new epitopes were characterized, the contractor should send a note explaining this.

Los Alamos National Labs (LANL) could handle the information in a variety of formats, and should be able to accommodate the needs of the researchers.

DATA REQUESTED:

1) Investigators that should be credited for the study.

2) The epitope sequence, based on the peptide sequence used to define the epitope.

3) The strain the peptide used to define the epitope (examples: MN, or autologous, or C consensus...)

4) The position of the epitope boundaries on the HXB2 reference strain (can be obtained using the HXB2 numbering engine at the HIV database website (www.hiv.lanl.gov).

5) The HLA presenting molecule of the epitope.

6) Very brief description of the experimental procedure used to define the epitope.

7) The complete set of HLA alleles of the individual(s) the epitope stimulated a response in.

8) Any information regarding mutations within the epitope: Does a substitution leave a response unaltered, does it confer escape, does it diminish a response? If an autologous sequence study is being conducted, a summary of cross-reactivity of different forms within the patient if known should be included.

9) The antigenic trigger of the CTL response that was measured – natural infection, vaccination... if vaccinated, what was the vaccine?

10) The subtype of the infecting virus, if known. (Or the subtype of the vaccine strain.)

11) The health status of the individual under study: recent seroconvertor, asymptomatic, AIDS, etc.

12) The city and country where the individual with the CTL response was living.

13) Year of sampling

14) Any further notes of interest the investigator would like to include, summarized in a few sentences. This would be study-specific elements that might be of interest. For example, was the epitope studied in mother-infant transmission cases? Was subtype cross-reactivity studied? Were all patients studied recent seroconvertors? Did this appear to be a dominant epitope?

LANL would also ask that the researchers notify us when the primary publications summarizing the epitopes are published, so we can be sure to get the updated information into the database. Also they should review the descriptions that appear on the database public web site to make sure it is accurate.

PART II: REACTIVE PEPTIDES:

LANL is beginning to get comprehensive sets of reactive peptides in, and will be publishing the first of these at our web site in collaboration with the University of Alabama for the Reach CTL Contract, upon acceptance of their initial CTL-response publication. Their paper is now ready for submission.

LANL is working with Harvard to get their reactive peptides in place, and will be working with them to design analysis tools to apply to them.

LANL believes there may be value in having these sets electronically available for cross-referencing by other researchers.

Therefore, upon publication of the papers describing CTL-stimulating peptides, as opposed to well-defined epitopes, LANL would like the researchers to submit to the database a table with the following elements:

1) All overlapping peptide sets used in the study
2) The HXB2 numbering system boundaries of the peptides
3) The number of individuals that reacted with a peptide
4) The HLA profiles of the individuals that reacted with the peptide

This should come with some background information describing the cohort, and the likely subtypes found in the cohort, and about the experimental procedure and peptide-set used to define CTL reactivities.

If researchers prefer to set up their own web site with this information, that would be fine. If they prefer to have LANL set up a web site with a link to the Medline abstract of their primary publication, this could also be accommodated. In either case, the information should be publicly electronically accessible upon publication.

Respecting patient privacy, ~~we~~ (LANL) does not want to get patient IDs, patient codes that researchers don't intend to put into publications, or precise dates of sampling, although the year of sampling is desirable.

Viral sequences should go to GenBank; LANL can pick it up from there. LANL would not do analysis with the sequences if LANL weren't part of the contract. It would be preferable that this be done at the time of annual reports.

Alternatively, researchers could submit to GenBank upon publication, as suggested for the Elispot data. They could send LANL a list of sequences and GenBank submission numbers including geographic origin, patient code, health status of the patient, risk factors, year sampled, co-receptor usage (if known) if NIAID requires that researchers ~~want to require they~~ go a bit further than a GenBank entry.

Except as provided herein, all terms and conditions of the RFP document NIH-NIAID-DAIDS-03-13 remain unchanged and in full force and effect. Offerors must acknowledge this Amendment #1, by acknowledging receipt of the amendment on each copy of the offer submitted. Failure to receive your acknowledgment of this amendment may result in the rejection of your offer.